Clinical Profile of Patients with Inflammatory Bowel Diseases in a Private Service

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Abstract

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory conditions affecting the digestive tract. This study examines 188 IBD patients in a private healthcare service in Canoas/RS, Brazil, aiming to understand their clinical profiles.

Most patients were young adults, primarily white, with more women affected. Both CD and UC patients commonly experienced diarrhea, but blood in stools was more prevalent in UC. CD mostly affected the small intestine, while UC involved the rectum or extended through the colon. The diagnosis was prompt, with most CD cases diagnosed within six months and UC cases within twelve months of symptom onset. Family histories of IBD and colorectal cancer were observed, particularly in CD patients. Extraintestinal manifestations were more frequent in CD. Elevated CRP levels were common in CD, while FC values were elevated in both groups. Treatment approaches differed, with 5-ASA primarily used in UC and immunomodulators in CD. Biological therapy was less commonly employed initially.

This study aligns with global IBD trends in demographics, symptoms, and disease locations. Early diagnosis likely results from specialized private healthcare, emphasizing the importance of timely diagnosis and tailored treatment.

Keywords

- Inflammatory bowel disease
- Crohn's disease
- Ulcerative colitis
- epidemiology
- incidence
- prevalence
- surgery

Introduction

Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are characterized by chronic and idiopathic inflammatory processes affecting the digestive tract. They primarily affect young individuals and, as chronic and recurrent diseases, result in structural damage that impairs the quality of life (QoL) of patients, both in the psychological and social domains, in addition to impacting morbidity and mortality.[1]

Although the etiology remains unknown, IBD is believed to be a multifactorial disease in genetically susceptible individuals, where there is an inadequate inflammatory response of the intestinal microbiota. IBD is more common in Western countries, such as Northern Europe and North America. However, there has been an increase in incidence and prevalence over the past two decades, especially in newly industrialized countries such as China, India, and Brazil.[2,3] The incidence of IBD increased from 9.4 in 2012 to 9.6 per 100,000 in 2020, and the prevalence increased from 30.0 in 2012 to 100.1 per 100,000 in 2020. In Rio Grande do Sul, the prevalence of IBD is 9.51 per 100,000 inhabitants, compared to 6.89 for Crohn's disease (CD) and 2.62 for ulcerative colitis (UC). The incidence of IBD is 1.61, with 1.17 for CD and 0.44 for UC.[4]

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The treatment depends on the severity of the disease, risk stratification, patient preference, and clinical factors, including age of onset, disease extent, and complications. Standard first-line therapeutic approaches include clinical treatments including corticosteroids, aminosalicylates and immunomodulators. Biologic agents are used in cases of treatment failure or for moderate to severe disease.[5] However, despite optimized medical therapy, approximately 9.2% of UC patients and 26.2% of CD patients still require surgery, either due to refractory disease to clinical treatment, associated complications, or the need for urgent interventions, with higher rates among cases of more severe and extensive disease.[6]

Objectives

General

To characterize and analyze the clinical and laboratory conditions of patients with IBD in outpatient care at a private specialized service in the city of Canoas/RS.

Specifics

1. Establish the profile of patients seen, including their symptomatic characteristics and laboratory findings;
2. Determine the time from symptom onset to the diagnosis of IBD;
3. Observe the presence of a family history of IBD and colorectal cancer (CRC) in IBD patients;
4. Observe the presence of extraintestinal manifestations in IBD patients.
5. Compare the types of initial treatment for CD vs. UC patients.

Methodology

This was a cross-sectional, observational, and descriptive study with an open population, conducted through the review of electronic medical records at a private specialized service in Canoas/RS. The sample included all patients aged 18 or older, under care at this institution since 2016, with the signing of informed consent forms (ICFs).

Statistical analysis was performed using the Pearson chi-square test in SPSS version 25. Statistical significance was considered when $P < 0.005$.

Results

A total of 188 patients were studied, with 101 having CD and 87 having UC. The vast majority were of the white race: 97% for CD and 95% for UC. CD was observed in younger patients compared to UC. Most CD patients were in the 20 to 40-year age group (59.4%), while UC patients (46.7%) were in the 20 to 50-year age group, with 26.7% being over 50 years old. Females were more affected in both pathologies, with a slight predominance in UC, but without statistical significance (59.4% vs. 73.3%, respectively). Perianal involvement was slightly higher in males (52.5%).

Regarding symptoms, diarrhea was present in more than half of the patients in both groups: 68.3% (CD) vs. 56.7% (UC). However, the presence of mucus and blood in the stools was statistically more significant in UC than in CD (45% and 61.7% vs. 19.8% and 34.7%, respectively).

Regarding location, according to the Montreal classification, one-third of CD patients were involved in the small intestine, primarily the terminal ileum (L1), 19% had ileocolonic disease (L3), 13% had exclusive colonic involvement (L2), and 8% had isolated perianal involvement (P). Perianal involvement was simultaneously present with small intestine involvement in 13%, with the colon in 7%, and with both the small intestine and colon in 12%. ►**Figure 1**. In UC, the rectum was the only segment affected in 27% of cases, with 25% involving only the distal third (Montreal classification E1); 13% extended to the sigmoid colon; 7% reached the splenic flexure (E2); and 10% affected all colonic segments, i.e., pancolitis (E3). ►**Figure 2**.

In 49.5% of CD cases, the diagnosis was made within 6 months of symptom onset, slightly higher for the perianal phenotype of CD (42.5%) compared to the luminal phenotype (39.3%). Only 2% required more than 24 months for confirmation. For UC, 56.7% had the diagnosis established within 12 months, with 30% of them within less than 6 months and 3.1% after more than 24 months. ►**Figure 3**.

A family history of IBD was more commonly observed in CD patients (14%) than in UC patients (7%), but without statistical significance. However, a family history of colorectal cancer (CRC) was low in both groups: 4% (CD) and 6% (UC). The presence of extraintestinal manifestations (EIM) was higher in the CD group (32.7%) than in the UC group (20%), but without statistical significance.

Biochemical changes assessed through C-reactive protein (CRP) were more commonly observed in CD patients ($> 50\%$) than in UC patients, where 60% had normal values. These findings were statistically significant ($P < 0.005$). However, fecal calprotectin (FC) values were elevated in many patients in both groups, without statistical difference. ►**Figure 4**.

Regarding treatment, immunomodulators, mostly represented by azathioprine, were used in 72.2% of CD patients vs. 16.7% in UC patients, with statistical significance. ►**Figure 5**. On the other hand, 5-aminosalicylates (5-ASA), primarily represented by mesalazine, both in oral (PO) and topical (PR)

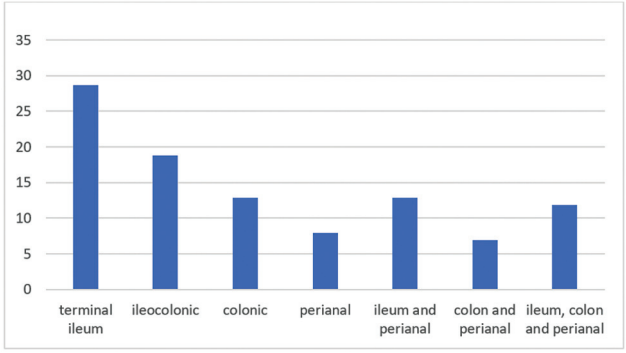

Fig. 1 Location of Crohn's Disease.

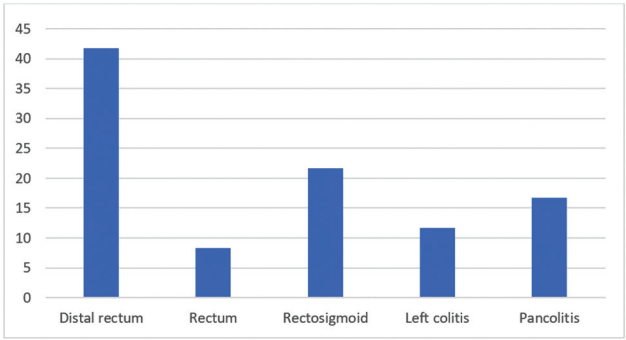

Fig. 2 Location of Ulcerative Colitis.

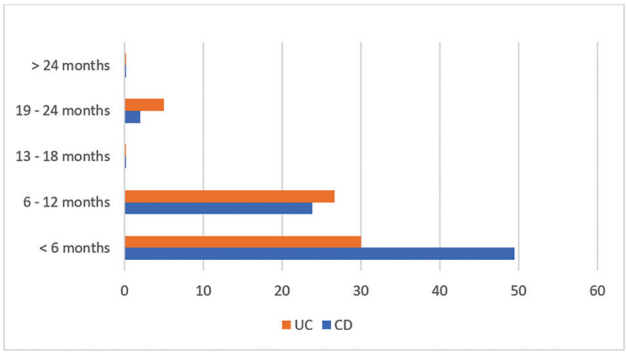

Fig. 3 Time relapsed from symptom onset to diagnosis.

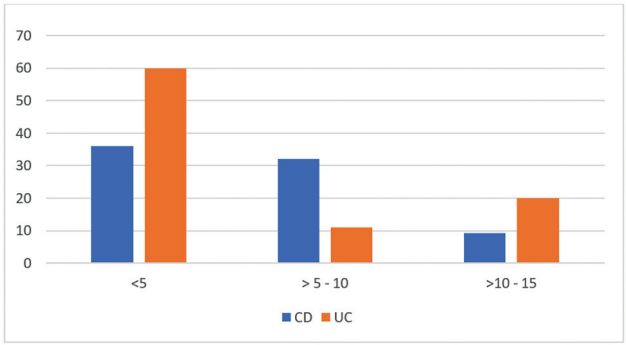

Fig. 4 CRP Value.

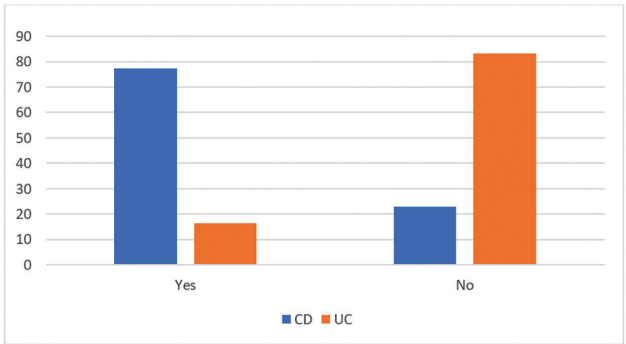

Fig. 5 Use of Azathioprine.

formulations, were used in almost all UC patients (83.3% and 85%, respectively) and in no cases of CD. Initial biological therapy with the anti-TNF infliximab was used in approximately one-third of CD patients (28.7%) and in only 3.3% of UC patients. The anti-TNF adalimumab was the first choice in approximately 40% of CD patients and in no cases of UC. The other representative of the anti-TNF class, certolizumab pegol, was the first option for 2% of CD patients. The anti-interleukin ustekinumab was the initial therapy in 11% of CD cases and in no cases of UC. Vedolizumab was the first choice in 6% of CD patients and, in no cases, the initial treatment in UC. Golimumab was not the initial option in any cases of UC. Budesonide was used in 3% of CD patients and in 1.7% of UC cases as the first option. ►**Figure 5**.

Discussion

Although the epidemiology of IBD is changing, it still has a high prevalence and incidence in individuals of European descent. Rio Grande do Sul has a population that self-identifies as white at 82.3%. Therefore, it was expected to find a predominance of white race in this study group. There was a predominance of females, consistent with what is observed in international and national literature.[7–9] The most affected age group was young adults: 20 to 40 years for CD and 30 to 50 years for UC, similar to what has been published nationally.[7,9]

A recent systematic review showed that achieving an immediate IBD diagnosis remains a challenging goal, with patients typically experiencing several months of delay in diagnosis. This is even worse for CD patients compared to UC, with most previous studies reporting a diagnostic delay of less than 12 months for CD compared to less than 6 months for UC. Particularly in publications about CD, one in four studies indicates that the average time between symptom onset and final CD diagnosis can take 12 to 24 months.[10] A recent meta-analysis observed that late CD diagnosis is associated with a higher risk of stenosis (OR = 1.88; 95% CI: 1.35–2.62), penetrating disease (OR = 1.64; 95% CI: 1.21–2.20), and intestinal surgery (OR = 2.24; 95% CI: 1.57–3.19). Conversely, for UC, a delayed diagnosis was associated with a higher risk of colectomy (OR = 4.13; 95% CI: 1.04–16.40).[11] In our study, due to it being conducted in a private referral service for IBD management, the diagnosis of CD in these patients was made within approximately six months of symptom onset in about half of them. As for UC, in 56.7% of patients, the time elapsed for diagnostic confirmation was up to 12 months, with no statistical difference between the two groups.

Regarding symptoms, a recent Spanish systematic review described rectal bleeding in UC and weight loss in CD as the most frequent. Diarrhea was the second most observed symptom.[12] However, our study identified that diarrhea was present in more than half of the patients in both groups, but the presence of blood in stools was statistically more significant in UC than in CD (61.7% vs. 34.7%, respectively).

In the Spanish CD study, the Montreal L1 location was more common in the adult and elderly population compared to the pediatric population, where the L3 location was more

frequent. Perianal disease was also more common in this age group. In UC, the E2 location was more frequent when compared to E1 and E3.12 In our study, the most common location in CD was also L1. However, in UC, location E1 was the most common.

From a biochemical perspective, according to Mahmoud H. Mosli et al., the sensitivity and specificity for C-reactive protein (CRP) are 0.49 (95% confidence interval (CI): 0.34-0.64) and 0.73 (95% CI: 0.66-0.79), respectively. For fecal calprotectin (FC), sensitivity and specificity are 0.92 (95% CI: 0.72-0.96) and 0.82 (95% CI: 0.73-0.88), respectively. FC was more sensitive than CRP in both diseases, and it was more sensitive in UC than in CD. In our study, elevated CRP was more commonly observed in CD patients than in UC patients, but FC was elevated in both pathologies.[13]

Overall, 12% of UC patients have a family history of IBD and are more likely to have a family history of UC than CD. Patients with pediatric-onset ulcerative colitis are more likely to have a family history of inflammatory bowel disease.[14] In a study of pediatric patients diagnosed with IBD, 25.2% had a positive family history. Moreover, these children had a higher risk of the stenosing phenotype than those with a negative family history, but no impact on IBD outcome.[15] In our study, a positive family history of IBD was more commonly observed in CD patients (14%) than in UC patients (7%).

There are studies suggesting an association between IBD and a susceptibility gene for CRC. Askling J. et al. observed a 3% family history of CRC in IBD patients in a cohort of approximately 20,000 patients. It is estimated that 2% of CRC diagnoses made each year are related to IBD.[16] A positive family history for CRC increases the risk of this cancer by at least two times compared to UC patients with no positive family history for CRC. The risk of CRC begins to increase 8 or 10 years after the IBD diagnosis is established. Patients with Crohn's colitis have a similar risk of developing CRC as UC patients.[17] In our study, a positive family history for CRC was present in 4% and 6% of CD and UC patients, respectively.

Extraintestinal manifestations (EIM) in CD and UC are common and can occur before or after the diagnosis of IBD. The frequencies range from 6% to 47%, and in approximately 25% of cases, they occur before the diagnosis of IBD. The median time for EIM to occur after IBD is 92 months, with a range of 29 to 183 months. 50% of IBD patients will have at least one EIM after 30 years from the IBD diagnosis. Perianal CD, smoking, and colonic involvement are risk factors.[18] In our study, the presence of EIM was higher in the CD group (32.7%) than in the UC group (20%). This finding may be justified by the fact that one-third of CD patients had perianal involvement in this studied cohort.

The treatment approach for UC differs from CD. The most used therapeutic class initially in moderate to severe UC is 5-aminosalicylate derivatives (5-ASA), mainly mesalazine. Immunomodulators (azathioprine or 6-mercaptopurine) are used in combination with mesalazine when there is no clinical, biochemical, or endoscopic remission with 5-ASA alone. Biological therapy is reserved for cases that fail conservative treatment (5-ASA and immunomodulators) or for severe cases.[3] That's why, in our study, mesalazine, both orally and topically, was used in more than 85% of UC patients. However, immunomodulators, mainly represented by azathioprine, were used in less than 20% of UC patients. Biological therapy, represented by anti-TNF infliximab, was used as a first-line drug in 3.3% of UC cases. Severe acute colitis occurs in 12-25% of UC patients, and the initial treatment is intravenous corticosteroids, In cases of failure, one of the options is infliximab.[3]

On the other hand, mesalazine is not recommended for inducing remission or promoting mucosal healing in CD patients. For cases of active ileocecal CD or disease limited to the ileum or mild to moderate ascending colon, budesonide can be used to induce remission. If treatment is ineffective, systemic corticosteroids should be used. Immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate) can be used as monotherapy for maintaining remission in CD patients who are dependent on and refractory to corticosteroids. It is recommended that patients refractory to immunomodulatory therapy or with complicated disease or poor prognosis characteristics be considered for early biological therapy.[2] In perianal CD, the incial strategy of treatment is biological therapy, preferably anti-TNF. The initial treatment strategies observed in our study are in accordance with the latest consensus from the Brazilian Organization of Crohn's Disease and Colitis (GEDIIB).

Conclusions

The analyzed cohort identified a similar number of CD and UC cases, with a predominance of young white women. Clinical, biochemical, and disease behavior findings, as well as therapeutic management, were like what is described in the literature. The most striking finding was the early nature of the diagnosis. This is probably justified by the fact that it is a cohort of patients from the private healthcare system, with care provided by a specialized IBD management service.

Conflict of Interest

The authors have no conflict of interests to declare.

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